

## REMARKS

Claims 1-12 and 14-23 are pending in the above-referenced application. Claims 1-6 have been amended to more distinctly claim the subject matter which Applicants regard as their invention and to advance prosecution. Applicants reserve the right to file subsequent continuation and/or divisional applications on subject matter originally recited in claim 1. Amended claims 1-6 are supported by the specification. No new matter has been added. Claims 7, 9, 10, 12 and 13 have been cancelled.

### 1. Priority Claim

It is asserted that the provisional application fails to provide adequate support under 35 U.S.C. 112 for claims 19, 21, and 23 of this application. Applicants respectfully disagree. The compounds recited in claim 19 are encompassed by the generic formula and specific substituents recited in the provisional application. Claims 21 and 23 depend from claim 23. Therefore, Applicants assert that claims 19, 21 and 23 are entitled to the priority date of the provisional application.

### 2. The Rejections Under 35 U.S.C. 103

Two obviousness rejections were made and are detailed below:

#### 2.1 The Rejection of Claims 1-12

Claims 1-12 and 14-16 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Pirotte et al. 5,459,138 in view of Nielsen et al. WO 97/26265. The Office Action specifically states:

Pirotte et al. teaches several process of making pyridinothiadiazinedioxide which include the processes a), b), c), and d) claimed in the instant claims. ...

Instant process claims require a thieno—fused 1,2,4-thiadiazinedioxide whereas the reference teaches pyridino-fused 1,2,4-thiadiazinedioxide.

The secondary reference Nielsen et al. WO97/26265, teaches the equivalency of thieno-fused 1,2,4-

thiadiazinedioxide with several heterocyclic ring fused thiadiazinedioxide including pyridino-fused thiadiazinedioxide. See formula I on page 3 and note the definition of A ring as well as D, B and other variable groups. Note various hetero-fused thiadiazines are enabled on pages 14-19. Also note the process on pages 21-25.

Note the starting material of the primary reference and the secondary reference are analogous and there is a clear-cut teaching in the secondary reference that the reaction that presence of different A ring does not alter the course of the process as the reaction centers are not affected by the presence of the different A ring.

Hence, one having ordinary skill in the art at the time of the invention was made would have been motivated combine the teachings of the primary reference with the teaching of the secondary reference and employ all the process parameters taught by these prior art including the process variation permitted and expect to obtain the desired product because he would have expected the analogous starting materials behave similarly under the reaction conditions taught by these prior art. It has been held that application of an old process to an analogous material to obtain a result consistent with the teachings of the art would have been obvious to one having ordinary skill.

The Office Action further states:

Applicants argue that compounds taught by Pirotte et al. are not [the] same as instant compounds. But instant claims are process claims and the reactive centers are just the same. Applicants have not shown that variation in the core A, i.e. thieno of instant [application] to pyridine taught by Pirotte et al. would alter the course of the reaction. Prior art of record does not support such a contention. Furthermore, applicants original claim 1 included so many variation in the A core yet was presented as viable process for all such cores. ..

Applicants respectfully traverse the rejection for a number of reasons. First, there is a significant difference between the compounds of Pirotte and the compounds made by the process recited in claim 1. Specifically, in Pirotte, the A core ring is limited to a

pyridine ring, whereas in the method of the present invention, A is defined as "A together with the carbon atoms forming bond *e* of formula I represents a 5 membered heterocyclic system comprising one or more nitrogen-, oxygen- or sulfur atoms...." A "5 membered heterocyclic system" is defined in the last paragraph of page 9 of the specification as:

..a monocyclic unsaturated or saturated system containing one two or three hetero atoms selected from nitrogen, oxygen and sulfur and having 5 members, e.g. pyrrole, furan, thiophene, pyrroline, dihydrofuran, dihydrothiophene, imidazole, imidazoline, pyrazole, pyrazoline, oxazole, thiazole, isoxazole, isothiazole, imidazoline, pyrazole, pyrazoline, oxazole, thiazole, isoxazole, 1,2,3-oxadiazole, furazan, 1,2,3-triazole, 1,2,3-thiadiazole or 2,1,3-thiadiazole.

This results in a significant difference in the chemical reactivity. It is well known that electron-deficient heterocycles like pyridines easily undergo nucleophilic substitution, while the electron-rich five-membered system such as those recited in I do not. Clearly, variation in the core A would alter the course of the reaction. Therefore, contra to assertions made in the Office Action, thieno-fused 1,2,4-thiadiazinedioxide would not be considered to be equivalent to pyridino-fused thiadiazine dioxide.

Applicants also note significant differences in the methods used to cyclize the starting materials. In the method recited in steps (a), (b) and (c) of amended claims 1-6, the compound of formula (IV) is cyclized in the solvent 2 in the presence of a metal catalyst. There was no such teaching or suggestion of the use of a metal catalyst in either of the cited references.

Applicants note that it is well established case law that a PTO rejection for obviousness is improper when there is nothing in the cited prior art references, either singly or in combination, to suggest the desirability of the claimed subject matter. *In re Deminski*, 796 F.2d 436, 230 USPQ 313 (Fed. Cir. 1986). If the teachings of two or more references are combined, there must be some logical reason or motivation, apparent from positive concrete evidence of record, which justifies a combination of primary and secondary references. *In re Regel* 526 F.2d 1399 (CCPA 1975). There would be no

motivation to combine the secondary reference, WO 97/26265 with Pirotte. *Contra* to the assertions made in the Office Action, WO97/26265 did not teach the equivalence of thieno-fused 1,2,4-thiadiazinedioxide "with several heterocyclic ring fused thiadiazinedioxide including pyridino-fused thiadiazinedioxide". Actually, WO97/26265 specifically excludes A forming a pyridine ring (see page 5, line 8). Furthermore, the methods disclosed to obtain the compounds in WO 97/26265 are very different from those disclosed in the instant application.

## **1.2 The Rejections of Claims 18-23**

Claims 18-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nielsen et al. WO 97/26265. The Office Action specifically states:

Teachings of Nielsen et al., as discussed in the above 103 rejection is incorporated herein. Nielsen et al. teaches several thieno-fused 1,2,4-thiadiazinedioxide as well as other heterocyclic ring fused thiadiazinedioxide for treating various diseases including diabetes. ....

Instant claims differs from Nielsen et al. in claiming specific species and species which are isomeric and their composition and method of use.

However, Nielsen et al. clearly teaches several isomeric thiadiazine dioxide.....Hence Nielsen et al. teaches equivalency of isomeric thiadiazines made with those generically claimed on page 3 for formula I. There is a clear-cut guidepost for making either of the isomeric thieno-thiadiazines. Thus, it would have been obvious to one having ordinary skill in the art at the time of the invention was made to make both the isomeric compounds variously substituted in thieno-thiadiazine ring as permitted by the reference and expect resulting compounds (instant compounds) to possess the uses taught by the art in view of the equivalency teaching outline above.

Applicants respectfully traverse the rejection. It is Applicants position that there is a disclosure of several compounds in WO 97/26265 spanning almost six pages. There

is no teaching as to which compounds would be optimal. Certainly the compounds recited in claims 18 and 19 are neither disclosed nor suggested. In Applicants view, making and using the claimed compounds would involve the improper use of hindsight and at best pose an "obvious to try" situation. An invention is merely "obvious to try" if the prior art gives either no indication of which parameters are critical or no direction as to which of many possible choices is likely to be successful. *Merck & Co., Inc. v. Biocraft Laboratories, Inc.*, 874 F.2d 804, 10 U.S.P.Q.2d 1843 (Fed. Cir. 1989). It is well known that the "obvious to try" standard is clearly erroneous. *In re O'Farrell*, 7 USPQ2d 1673 (Fed. Cir. 1988).

In view of the above arguments and the amendments of claims 1-6, Applicants assert that the rejections under 35 U.S.C. 103(a) have been overcome. Therefore, Applicants respectfully request that the rejections be withdrawn.

### 3. The Double Patenting Rejection

Claims 18-23 have been rejected under the judicially created doctrine of obviousness-type double patenting over claims 1-31 of U.S. Patent No. 5,889,002 and claims 1-25 of U.S. Patent No. 6,329,367. It is asserted that both of the references teach nonofused-1,24-thiadizine, composition and method of use which overlaps with the instant claimed composition.

Applicants respectfully traverse the rejection. As conceded in the Office Action, the cited prior art patents do not teach the compounds recited in claims 18 and 19. It is Applicants view that the compounds recited in claims 18 and 19 are patentably distinct from those encompassed by claims 1-31 of U.S. Patent No. 5,889,002 and claims 1-25 of U.S. Patent No. 6,329,367. Applicants point out that the fact that a claimed compound may be encompassed by a disclosed generic formula does not by itself render that compound obvious. *In re Jones*, 958 F.2d 347, 350, 21 USPQ2d 1941, 1943 (Fed. Cir. 1992). A reference must be considered not only for what it expressly teaches, but also for what it fairly suggests. *In re Burckel*, 592 F.2d 1175, 1179, 201 USPQ 67, 70 (CCPA

1979). The formulae recited in U.S. Patent Nos. 5,889,002 and 6,329,367 encompasses many different compounds. Therefore, *contra* to the assertion made in the Office Action, one of ordinary skill in the art would not have had a reasonable expectation of success that the compounds recited in claims 18-19 of the instant application could necessarily be used to treat type I or II diabetes.

In view of the above arguments, Applicants assert that the double patenting rejections have been overcome. Therefore, Applicants respectfully request that the rejections be withdrawn.

#### 4. Conclusions

In view of the above, it is respectfully submitted that all of the pending claims are in condition for allowance. Early action to that end is respectfully requested. The Examiner is hereby invited to contact the undersigned by telephone at (914) 712-0093 if there are any questions concerning this amendment or application.

Respectfully submitted,

Date:

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